transcription of a gene having a transcriptional regulatory element to which the DNA binding domain binds.

23. (Amended) A nucleic acid composition comprising at least two genetic constructs, each encoding a chimeric protein,

(a) a first construct encoding a first chimeric protein comprising at least one ligand-binding domain and a signal initiation domain which is heterologous thereto; and,

(b) a second construct encoding a second chimeric protein comprising at least one ligand-binding domain which may be the same or different from a ligand binding domain of the first chimeric protein, and an intra-cellular localization domain,

wherein the first and second of said chimeric proteins together (i) bind to a ligand to form a ligand cross-linked protein complex, and (ii) in a ligand dependent manner, activate an intra-cellular signaling pathway.

Please add the following new claims:

49. (New) A nucleic acid composition comprising at least two genetic constructs, each encoding a chimeric protein,

(a) a first construct encoding a first chimeric protein comprising at least one ligand-binding domain, a signal initiation domain which is heterologous thereto, and a cytoplasmic domain of a cell surface receptor; and,

(b) a second construct encoding a second chimeric protein comprising at least one ligand-binding domain which may be the same or different from a ligand binding domain of the first chimeric protein, a signal initiation domain which may be the same or different from a signal initiation domain of the first chimeric protein, and a cytoplasmic domain of a cell surface receptor which may be the same or different from a cytoplasmic domain of a cell surface receptor of the first chimeric protein,

wherein the first and second of said chimeric proteins together (i) bind to a ligand to form a ligand cross-linked protein c mplex, and (ii) in a ligand dependent manner, activate a cellular signaling pathway.

50. (New) The composition of claim 23, wherein the intra-cellular localization domain is a nuclear localization domain.

51. (New) The composition of claim 23, wherein the intra-cellular localization domain is a cytoplasmic localization domain.

52. (New) The composition of claim 23, wherein the intra-cellular localization domain comprises a secretory leader sequence, a membrane retention domain, a nuclear localization domain, or a vesicle targeting domain.

53. (New) The composition of claim 52, wherein the membrane retention domain comprises a plasma membrane targeting sequence for attachment of a myristoyl moiety or a prenyl moiety.

54. (New) The composition of claim 49 in which the ligand-binding domain of at least one of the chimeric proteins is an FKBP domain.

55. (New) The composition of claim 49 in which the ligand-binding domain of at least one of the chimeric proteins is a variant of an FKBP domain.

56. (New) The composition of claim 49, wherein at least one of the ligand-binding domains comprises FKBP12 or a variant thereof in which one or more of Tyr26, Phe36, Asp37, Tyr82 and Phe99 are replaced by other amino acid residues.

57. (New) The composition of claim 49 in which the ligand binding domain of at least one of the chimeric proteins specifically binds to FK506, FK520, rapamycin, or a derivative of either.

58. (New) The composition of claim 49 in which the cytoplasmic domain of a cell surface receptor is selected from the group consisting of a tyrosine kinase receptor, a cytokine receptor and a growth factor receptor.

59. (New) The composition of claim 49 in which the cytoplasmic domain of a cell surface receptor is selected from the group consisting of a Fas receptor and a TNF receptor.

60. (New) The composition of claim 22 in which the ligand-binding domain of at least one of the chimeric proteins is an FKBP d main.

61. (New) The composition of claim 22 in which the ligand-binding domain of at least one of the chimeric proteins is a variant of an FKBP domain.

62. (New) The composition of claim 22, wherein at least one of the ligand-binding domains comprises FKBP12 or a variant thereof in which one or more of Tyr26, Phe36, Asp37, Tyr82 and Phe99 are replaced by other amino acid residues.

63. (New) The composition of claim 22 in which the ligand binding domain of at least one of the chimeric proteins specifically binds to FK506, FK520, rapamycin, or a derivative of either.

64. (New) A eukaryotic cell containing and capable of expressing at least one nucleic acid construct of claim 22, 23, or 49.

65. (New) The composition of claim 23 in which the ligand binding domain of at least one of the chimeric proteins is an FKBP domain.

66. (New) The composition of claim 23 in which the ligand-binding domain of at least one of the chimeric proteins is a variant of an FKBP domain.

67. (New) The composition of claim 23, wherein at least one of the ligand-binding domains comprises FKBP12 or a variant thereof in which one or more of Tyr26, Phe36, Asp37, Tyr82 and Phe99 are replaced by other amino acid residues.

68. (New) The composition of claim 23 in which the ligand binding domain of at least one of the chimeric proteins specifically binds to FK506, FK520, rapamycin, or a derivative of either.

69. (New) The composition of claim 23 or 49 in which the activation of a cellular signaling pathway regulates, in a ligand dependent manner, at least one of cell proliferation, differentiation, or death.

The amended claims are re-stated bel w to reflect changes with respect to the last filing.

14. **(Twice Amended)** A ~~DNA~~ vector ~~containing~~ including a DNA construct of claim 22 ~~1~~ and a selectable marker permitting transfection of the DNA construct into host cells and selection of transfectants containing the construct.

18. **(Amended)** A mammalian cell ~~containing and capable of expressing~~ which contains and expresses at least one ~~DNA~~ nucleic acid construct of ~~any of claims 1-13~~ claim 22, 23 or 49.

22. **(Amended)** A ~~DNA~~ nucleic acid composition comprising at least two genetic constructs, each encoding a chimeric protein,

(a) a first ~~DNA~~ construct encoding a first chimeric protein comprising ~~(i)~~ at least one ligand-binding domain and a transcriptional activation domain which is heterologous thereto, ~~receptor domain, capable of binding to a selected ligand, fused to (ii) a heterologous additional protein domain capable of initiating a biological process upon exposure to the ligand; and~~

(b) a second ~~DNA~~ construct encoding a second chimeric protein comprising at least one ligand-binding domain which may be the same or different from a ligand binding domain of the first chimeric protein, and a DNA binding domain, ~~target gene under the transcriptional control of an transcriptional control element responsive to the oligomerization of a protein.~~

wherein the first and second of said chimeric proteins together (i) bind to a ligand to form a ligand cross-linked protein complex, and (ii) in a ligand dependent manner, activate transcription of a gene having a transcriptional regulatory element to which the DNA binding domain binds.

23. **(Amended)** A ~~DNA~~ nucleic acid composition comprising at least two genetic constructs, each encoding a chimeric protein,

(a) a first ~~DNA~~ construct encoding a first chimeric protein comprising ~~(i)~~ at least one ligand-binding d main and a signal initiation domain which is ~~first receptor domain, capable of binding to a selected first ligand moiety, fused to (ii) a~~

heterologous thereto ~~additional protein domain capable of initiating a biological process upon exposure to the ligand in the presence of a second chimeric protein~~; and,

(b) a second ~~DNA~~ construct encoding ~~the~~ a second chimeric protein comprising ~~(i)~~ at least one ~~receptor~~ ligand-binding domain which may be the same or different from a ligand binding domain of the first chimeric protein, and an intra-cellular localization domain, ~~capable of binding to a selected second ligand moiety, fused to (ii) a heterologous additional protein domain capable of initiating a biological process upon exposure to the ligand in the presence of the first chimeric protein;~~

wherein the first and second of said chimeric proteins together (i) bind to a ligand to form a ligand cross-linked protein complex, and (ii) in a ligand dependent manner, activate an intra-cellular signaling pathway. ~~the first and second receptor moieties may be the same or different and the first and second selected ligand moieties may be the same or different; and~~

~~(c) a target DNA construct encoding a target gene under the transcriptional control of a transcriptional control element responsive to the oligomerization of a chimeric protein.~~

REMARKS

Claims 1, 6, 14, 17, 18, 20-24, 30-33, 36-39, 45 and 48 were the pending claims in the present application. Claims 1, 6, 14, 18, 20-23, 31, 36-39 and 45 were elected with traverse. Applicants have canceled non-elected claims. Applicants also cancel, without prejudice, claims 1, 6, 20, 21, 31, 36, 37, 38, 39 and 45. Applicants add new claims 49-69. Support for the subject of these claims is found throughout the specification. No new matter has been added. Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

1-3. Applicants note the Examiner's acknowledgement of the election of Group I in Paper 11. However, Applicants reiterate that the election of Group I was an election with traverse.